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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/661,629	09/15/2003	Thomas J. Jentsch	2815-0236P	9386

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BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
BALLARD, KIMBERLY A	
ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 09/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/661,629	JENTSCH, THOMAS J.	
	Examiner	Art Unit	
	Kimberly A. Ballard	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) *1-12 and 20-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13 and 15-19* is/are rejected.

7)☒ Claim(s) *14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/590,304.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/15/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II, claims 13-19, drawn to polypeptides, in the reply filed on July 26, 2006 is acknowledged. The species election of neurodegenerative diseases, elected with traverse, is also acknowledged. In a phone interview on September 8, 2006 with Applicant's agent, Thomas Siepmann, Ph.D., it was acknowledged that Applicant further elects to prosecute SEQ ID NO: 2, with traverse. The traversals are on the ground(s) that: 1) with regard to Groups II and V, these groups are drawn to the exact same classification, so searching these groups together would not be a burden and therefore the groups should combined. 2) With regard to Groups I and II, Applicant argues that the subject matter of Group I are nucleic acids which actually encode the peptides of Group II, thus searching for one group encompasses searching the other and would not be an undue burden on the Office. Therefore Applicant asserts that the restriction requirement for Groups I and II should be withdrawn. 3) As for the secondary restriction requiring election of a specific polypeptide sequence, Applicant traverses on the grounds that such restriction should be a species election instead. And 4), as for the species election requiring election of a specific disease recited in claims 42 and 50, Applicant traverses based on the grounds provided above, with respect to Groups I, II, and V.

This is not found persuasive because the similar classifications for groups II and V are not absolutely binding, as evidenced by the recitation "classified for example in

class 530, subclass 350." While the classification for Group II may indeed be 530/350 because the group is drawn to polypeptides, the classification for the "chemical compound" of Group V (claim 41) cannot be fully determined because it is a compound found by the screening method of claim 37 and therefore is the compound is not known or explicitly recited, and could include, for example, an antibody (classified for example in 530/387.1), an organic compound (classified for example in 514/1), or even a inorganic agent (classification dependent on structure). Accordingly, there would be a substantial burden placed upon the Office to examine the inventions of groups II and V together. An application may properly be required to be restricted to one of two or more claimed inventions if they are able to support separate patents and they are either independent (MPEP § 806.04 – § 806.04(j)) or distinct (MPEP § 806.05 – § 806.05(i)). With regard to point 2), the Examiner has shown that groups II and I are independent or distinct for the reasons in the previous Office action (see Paper mailed 06/26/2006). Furthermore, MPEP § 803 provides that the separate classification (i.e., class and subclass) of distinct inventions is sufficient to establish a *prima facie* case that the search and examination of the plural inventions would impose a serious burden upon the Examiner; such separate classification was set forth in the Restriction requirement mailed 06/26/2006. With regard to point 3), as noted in the 06/26/2006 Restriction requirement, each of the polypeptides has a unique structural feature that requires a unique search of the prior art. The polypeptides of SEQ ID NOS: 2-10 differ in structure and function as they are composed of divergent amino acids and are differentially able to bind or mediate biological functions. A reference to one element would not constitute

a reference to another. In addition, searching all of the molecules in a single patent application would provide an undue search burden on the examiner and the USPTO's resources because the indicated searches are not co-extensive. And finally, with regard to point 4), the species election requirement is rendered moot because the elected claims do not recite nor require the disease species designated in non-elected claims 42 and 50, and therefore the species election is hereby withdrawn.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-12 and 20-52 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on July 26, 2006.

Accordingly, claims **13-19** are under examination in the instant office action.

The Examiner of U.S. Patent Application No. 10/661,629 has changed. In order to expedite the correlation of papers with the application, please direct all future correspondence to Examiner Ballard, Technology Center 1600, Art Unit 1649.

Information Disclosure Statement

A signed and initialed copy of the IDS paper submitted 09/15/2003 enclosed in this action.

Specification

The disclosure is objected to because of the following informalities: The status of the parent divisional application 09/590,304 in the first paragraph of the specification needs to be updated to reflect its issuance as US Patent No. 6,649,371.

Appropriate correction is required.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed, regarding potassium channel KCNQ5 polypeptides. Additionally, it is suggested that Applicant omits the word "NOVEL" from the title. Novelty is a legal concept and does not describe the invention claimed. Novelty is required of all claimed inventions before they are issued as patents. To use the term in the title would imply merit in the regard without actual examination. Accordingly, though MPEP 606.01 does not specifically refer to "novel", it is similar to the term "improve" which also implies merit without examination.

Sequence Requirements

In order to have compact prosecution a first office action can be performed on this application, however, this application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). This application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825. The disclosure contains sequences that

require SEQ ID numbers, particularly on pages 9-12, Table 1, and page 12, lines 25-28. Applicant is reminded to check the entire disclosure to ensure that the application is in sequence compliance.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13, 15, 17 and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a recombinantly produced polypeptide comprising SEQ ID NO: 2 or the variant KCNQ5/G278S, does not reasonably provide enablement for any recombinantly produced polypeptide comprising all or a portion of a human, rat or murine KCNQ5 protein or any KCNQ5 variant. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

Claim 13 is drawn to a recombinantly produced polypeptide comprising all or a portion of a human, rat or murine KCNQ5 protein. Claim 15, as it depends from claim 13, adds the limitation that the polypeptide comprises a molecular weight of approximately 99 kDa. Claims 17 and 18 are drawn to KCNQ5 variants, wherein said variant has an amino acid sequence that has been changed by addition, deletion, or substitution of one or more amino acids, and wherein such changes are located in conserved regions, as defined by Table 1. The claims thus broadly encompass a multitude of protein portions and protein variants.

Applicant has disclosed only one amino acid sequence, SEQ ID NO: 2, which encodes the KCNQ5 protein (a potassium channel subunit), and five variant sequences: four splice variants at positions 432-476 (KCNQ1 numbering) and the KCNQ5/G278S variant, which has a substituted serine for a glycine at position 278 (KCNQ5 numbering) (p. 12, lines 23-30). Table 1 of the instant specification lists the amino acid sequences of human KCNQ1 – KCNQ5, and also denotes conserved amino acid residues within these sequences, wherein over 180 conserved amino acids are indicated. According to the claimed variant protein, any one of these 180 amino acids may be changed (i.e., added, deleted, or substituted), and there is no limit as to how many *other* amino acid residues may be changed in addition to that one amino acid. Therefore, the scope of the instantly claimed polypeptide encompasses a multitude of potential KCNQ5 variants, as well as portions of the KCNQ5 protein, for which detailed structural and functional information is lacking. One of skill in the art would thus not be able to predict which portions of the KCNQ5 protein or which KCNQ5 variant would meet the

limitations of the claims. And even though a suitable assay is provided for examining the functional activity of the KCNQ5 variant polypeptides, it would require undue experimentation of the skilled artisan to screen such a large number or variant polypeptides, particularly when the expectation of obtaining the desired activity is unpredictable.

It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. As an example of the unpredictable effects of mutations on potassium channel protein function, Schwake et al. (*J Neurosci*, 2006; 26(14): 3757-3766) demonstrate that deletion or mutation of one of two coiled-coil motifs in either KCNQ2 or KCNQ3 proteins abolished or disrupted channel activity after expressing the proteins singly (homomeric channel) or in combination with (heteromeric channel) other KCNQ proteins (see pp. 3761-3762 and Figures 5 and 6). Additionally, it is recognized in the art that single amino acid mutations within a protein's amino acid sequence can lead to disease conditions resulting from abnormal protein function. For example, Castaldo et al. (*J Neurosci*, 2002; 22(2): RC199, 1-6) notes that a single arginine to tryptophan substitution (R214W) in the related KCNQ2 protein leads to a rare generalized epilepsy of newborns known as benign familial neonatal convulsions (BFNC). And Jentsch (*Nat Rev Neurosci*, 2000; 1: 21-30) notes that "mutations in four out of five KCNQ genes underlie diseases including cardiac arrhythmias, deafness and epilepsy." Thus, the art recognizes that changes to a KCNQ protein's amino acid sequence can lead to significant and unpredictable functional outcomes.

Since the claims encompass proteins potentially containing mutations and/or modifications and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The instant claims set forth no structural or functional limitations with which to identify the KCNQ5 protein from the myriad of potential variants that could be considered KCNQ5 proteins. Since detailed information regarding the structural and functional requirements of the protein are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Thus, since Applicant has not disclosed how to recognize such protein variants or portions of such proteins, it would require undue experimentation for one of skill in the art to make and use the claimed protein portions or variants in their full scope.

Claims 13, 15, 17, and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Factors to be considered when determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of

making the claimed invention. (Written description guidelines, Federal Register, vol. 66, no. 4, January 2002, 9.1106, column 2).

Claim 13 is broadly drawn to a recombinantly produced polypeptide comprising all or a portion of a human, rat or murine KCNQ5 protein. Claim 15, as it depends from claim 13, adds the limitation that the polypeptide comprises a molecular weight of approximately 99 kDa. Claims 17 and 18 are broadly drawn to KCNQ5 variants, wherein the variant contains amino acid additions, deletions, or substitutions at one or more positions. Claims 13, 15, 17, and 18 are thus drawn to a genus of protein portions and variants, and are genus claims.

A description of a genus may be achieved by means of a recitation of a representative number of members, defined by structure and/or function, falling within the scope of the genus, or of a recitation of structural and/or functional features common to the genus, which features constitute a substantial portion of the genus. However, Applicant has disclosed only one amino acid sequence, SEQ ID NO: 2, which is the KCNQ5 protein, and five additional KCNQ5 variants: four splice variants with alternative splicing at positions 432-476 (KCNQ1 numbering) and one "preferred" variant KCNQ5/G278S, which has a substituted serine for a glycine at position 278 (KCNQ5 numbering) (p. 12, lines 23-30). Table 1 of the instant specification denotes conserved amino acid residues within the KCNQ5 sequence, wherein over 180 conserved amino acids are indicated. The specification and claims, therefore, do not place a limit on the number of conserved amino acid residue substitutions, deletions, insertions and/or additions that may be made to obtain the KCNQ5 variant species.

Further, there is no recited functional limitation with regard to a "portion of a KCNQ5 protein," and structural features that could distinguish these polypeptide portions in the genus from others in the amino acid class are missing from the disclosure. The scope of the claimed invention is thus so broad that the skilled artisan would not be able to envisage the entire genus claimed of polypeptides that would qualify as KCNQ5 proteins or portions of the protein, and further the skilled artisan would not recognize that the applicant was in possession of the claimed invention at the time of filing.

The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Given the broad scope of the instantly claimed polypeptides, and the fact that the specification provides limited guidance regarding the structural and functional features of variant KCNQ5 polypeptides and portions thereof, one of skill in the art would reasonably conclude that Applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13 and 15-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 is vague and indefinite in so far as it employs the term "KCNQ5" protein as a limitation. Without a reference to a precise amino acid sequence identified by a proper SEQ ID NO: one cannot determine the metes and bounds of a "recombinantly produced protein...comprising all or a portion of a human, rat or murine KCNQ5 protein." Moreover, because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a "KCNQ5" protein, an artisan cannot determine if a compound which meets all the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation.

Claims 15-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for being dependent from indefinite rejected claim 13.

Claim 18 recites the limitation "the conserved regions" in lines 2-3 of the claim. There is insufficient antecedent basis for this limitation in the claim.

Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as it recites the limitation "as defined by Table 1". With regard to references to figures and tables in a claim, the MPEP § 2173.05(s) states:

Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." Ex parte Fressola, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993) (citations omitted).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 13 is rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,403,360 B1 to Blanar et al., issued June 11, 2002, filed June 26, 1998.

The claim is drawn to a recombinant polypeptide comprising all or a portion of a human, rat, or murine KCNQ5 protein.

Blanar et al. teach KCNQ2 and KCNQ3 proteins and teach the amino acid sequence RXXQXXRXXR (SEQ ID NO: 25), wherein X is any amino acid, and which is defined as the signature sequence for a potassium channel (see columns 57-58). The

instant KCNQ5 protein (SEQ ID NO: 2 of the instant application) comprises the above SEQ ID NO: 25 (residues 201-210 of SEQ ID NO: 2). SEQ ID NO: 25 would thus anticipate instant claim 13 as the sequence is a portion of a KCNQ5 protein.

Claim Objections

Claim 13 objected to because of the following informalities: claim 13 depends from withdrawn claim 1. Appropriate correction is required.

Conclusion

Claims 13 and 15-19 are rejected.

Claim 14 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Ballard whose telephone number is 571-272-4479. The examiner can normally be reached on M-F 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kimberly Ballard, Ph.D.
September 21, 2006